Original Article

Study of Clinical Profile and Inflammatory Markers in Children Between 2 Months and 12 Years of Age with Influenza-Like Illness: A Hospital-Based Study

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Abstract

Background: Influenza-like illness (ILI) is a common cause of pediatric outpatient visits and hospital admissions. During the COVID-19 pandemic, differentiation between COVID-19, influenza, and other respiratory illnesses became increasingly important due to similarities in clinical presentation. Assessment of inflammatory biomarkers may assist in evaluating disease severity and predicting outcomes. The aim is to study the clinical profile and inflammatory markers in children aged 2 months to 12 years presenting with influenza-like illness in a tertiary care teaching hospital. **Material and Methods:** This cross-sectional hospital-based study was conducted in the Department of Pediatrics at MGM Hospital, Kamothe, from August 2022 to December 2023. A total of 75 children aged 2 months to 12 years presenting with ILI symptoms were enrolled consecutively after obtaining informed consent. Rapid antigen tests were performed for influenza and COVID-19. Clinical characteristics, laboratory investigations, inflammatory markers, radiological findings, disease severity, and outcomes were recorded. Statistical analysis was performed using IBM SPSS software. A p-value <0.05 was considered statistically significant. **Results:** Among 75 children, 62 (82.67%) were diagnosed with other ILI, 9 (12%) with influenza, and 4 (5.33%) with COVID-19. The majority belonged to the 1–5-year age group (40%). Fever was present in all children, while cough (89.33%) and rhinorrhea (86.67%) were common symptoms. Loss of taste and smell were significantly associated with COVID-19 (p<0.001). Respiratory distress was significantly more common in COVID-19 and influenza cases (p<0.001). Oxygen saturation was significantly lower in COVID-19 and influenza patients (p=0.028). Bilateral infiltrates on chest radiography were significantly associated with COVID-19 and influenza (p=0.003). Raised CRP was observed in 69.34% of cases but did not significantly differ among disease categories. All patients showed clinical improvement during follow-up. **Conclusion:** Most children presenting with ILI had non-COVID, non-influenza illnesses. Loss of smell and taste, respiratory distress, lower oxygen saturation, and bilateral radiological infiltrates were significantly associated with COVID-19 and influenza infections. Inflammatory markers demonstrated limited discriminatory value between disease categories but may assist in monitoring disease progression.

Keywords: Influenza-like illness, COVID-19, Influenza, Children, Inflammatory markers, CRP, Pediatric respiratory infections.

Received: 12 May 2026 **Revised: 22 May 2026** **Accepted: 06 June 2026** **Published: 10 June 2026**

Introduction

Influenza-like illness (ILI) is a clinical syndrome characterized by fever accompanied by respiratory symptoms such as cough, sore throat, rhinorrhea, nasal congestion, or difficulty breathing. It represents one of the most common reasons for pediatric healthcare visits worldwide and contributes significantly to morbidity, hospitalization, school absenteeism, and healthcare expenditure. Children play an important role in the transmission of respiratory viral infections because of close interpersonal contact and relatively immature immune responses.[1,2]

Respiratory viral infections in children are caused by a wide variety of pathogens including influenza viruses, respiratory syncytial virus (RSV), adenovirus, parainfluenza virus, rhinovirus, human metapneumovirus, and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Although these infections often present with similar clinical manifestations, disease severity and outcomes may vary considerably depending on the causative organism, host immune response, and associated comorbidities.[3,4]

The emergence of the COVID-19 pandemic posed unprecedented challenges to healthcare systems globally. Children generally experience milder COVID-19 disease than adults; however, severe manifestations including pneumonia, acute respiratory distress syndrome, and multisystem inflammatory syndrome in children (MIS-C) have been reported. Since COVID-19 and influenza share many overlapping clinical

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DOI:
10.21276/amit.2026.v13.i2.731

How to cite this article: Nagargoje RV, Kamale V. Study of Clinical Profile and Inflammatory Markers in Children Between 2 Months and 12 Years of Age with Influenza-Like Illness: A Hospital-Based Study. Acta Med Int. 2026;13(2):609-613.

features, differentiation based solely on symptoms is often difficult. Accurate identification is essential for infection control, isolation measures, and appropriate treatment strategies.[5,6]

Inflammatory markers have gained increasing attention as indicators of disease severity and prognosis in respiratory infections. Biomarkers such as C-reactive protein (CRP), ferritin, D-dimer, procalcitonin, leukocyte counts, and lymphocyte counts reflect the host inflammatory response and may provide valuable information regarding disease progression. Elevated inflammatory markers have been associated with severe COVID-19 and complicated influenza infections in both adults and children.[7,8]

Several studies have demonstrated that CRP and procalcitonin may help distinguish viral from bacterial infections, whereas ferritin and D-dimer have been linked to hyperinflammatory states and thrombotic complications. However, data regarding the utility of these biomarkers in pediatric patients with ILI remain limited, particularly in developing countries.[9,10]

India experienced substantial pediatric respiratory disease burden during and after the COVID-19 pandemic. The simultaneous circulation of influenza viruses and SARS-CoV-2 has increased the complexity of diagnosis and management. Understanding the clinical characteristics and inflammatory marker profiles among children presenting with ILI can facilitate early risk stratification and optimize healthcare resource utilization.[11]

Therefore, the present study was undertaken to evaluate the clinical profile, disease severity, laboratory findings, inflammatory markers, radiological features, and outcomes among children aged 2 months to 12 years presenting with influenza-like illness and to compare findings among COVID-19, influenza, and other ILI groups.[12]

Materials and Methods

Study Design: A hospital-based cross-sectional observational study was conducted.

Study Setting: The study was carried out in the Pediatric Outpatient Department (OPD), Pediatric Ward, Emergency Department, and Pediatric Intensive Care Unit (PICU) of MGM Hospital, Kamothe, Navi Mumbai.

Study Duration: The study was conducted from 1 August 2022 to 31 December 2023. Data analysis and dissertation preparation were completed between January 2024 and May 2024.

Study Population: Children aged between 2 months and 12 years presenting with influenza-like illness symptoms constituted the study population.

Sample Size: A total sample size of 75 children was calculated using the formula:

n=\frac{4PQ}{L^2}

where:

- P = 50%
- Q = 50%
- Confidence level = 95%
- Margin of error = 12%

Inclusion Criteria

- Children aged 2 months to 12 years.
- Presence of influenza-like illness symptoms including:
  - Fever
  - Cough
  - Rhinorrhea
  - Nasal congestion
  - Sore throat
  - Sneezing
  - Chills
  - Headache

Exclusion Criteria

- Congenital craniofacial anomalies such as cleft lip and cleft palate.
- Immunodeficiency disorders.
- Children receiving immunosuppressive therapy.
- Refusal of parental consent.

Ethical Approval

The study was approved by the Institutional Ethics Committee of MGM Medical College and Hospital.

Approval Number: DHR-EC/2022/SC/08/86

Written informed consent was obtained from parents or guardians prior to enrollment.

Study Procedure

All eligible children underwent:

Clinical Evaluation

- Detailed history
- General physical examination
- Respiratory system examination
- Assessment of disease severity

Diagnostic Testing

Rapid antigen testing was performed for:

- Influenza A and B using Accucare One Step Influenza A+B Rapid Test Kits
- COVID-19 using Covifind Rapid Test Kits (Meril Diagnostics)

Children negative for influenza were subsequently tested for COVID-19.

Laboratory Investigations

The following investigations were performed according to clinical indication:

- Complete blood count
- Hemoglobin
- Total leukocyte count
- Differential leukocyte count
- Platelet count
- C-reactive protein
- D-dimer
- Ferritin
- Procalcitonin

Radiological Assessment: Chest radiography was performed in children with moderate or severe disease or when clinically indicated.

Disease Classification

Patients were categorized into:

1. COVID-19 infection
2. Influenza infection
3. Other Influenza-Like Illnesses

Severity was classified as:

- Mild
- Moderate
- Severe

according to national and international guidelines.

Outcome Assessment

Clinical outcomes included:

- Improvement
- Deterioration
- Need for hospitalization
- PICU admission
- Mortality
- Discharge status

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics Version 25.0 (IBM Corp., Armonk, New York, USA).

Continuous variables were expressed as Mean ± Standard Deviation.

Categorical variables were expressed as frequencies and percentages.

Statistical tests used:

- Unpaired Student's t-test
- Chi-square test
- Fisher's Exact test when appropriate

A p-value <0.05 was considered statistically significant.

Results

Among 75 children, Other ILI was most common, seen in 62 cases (82.67%), followed by influenza in 9 cases (12%) and COVID-19 in 4 cases (5.33%). The maximum number of children belonged to the 1–5 years age group, 30 (40%), followed by 6–12 years, 26 (34.67%), and up to 1 year, 19 (25.33%). Age distribution was not statistically significant (p=0.963). Males constituted 44 (58.67%) and females 31 (41.33%), with no significant gender association (p=0.911).

Table 1: Demographic profile and diagnosis-wise distribution

Variable	COVID n (%)	Influenza n (%)	Other ILI n (%)	Total n (%)	p value
Up to 1 year	1 (1.33)	2 (2.67)	16 (21.33)	19 (25.33)	0.963
1–5 years	1 (1.33)	4 (5.33)	25 (33.34)	30 (40.00)	
6–12 years	2 (2.67)	3 (4.00)	21 (28.00)	26 (34.67)	
Female	2 (2.67)	4 (5.33)	25 (33.33)	31 (41.33)	0.911
Male	2 (2.67)	5 (6.67)	37 (49.33)	44 (58.67)	

Table 2: Clinical presentation and severity

Parameter	COVID n (%)	Influenza n (%)	Other ILI n (%)	Total n (%)	p value
Fever present	4 (5.33)	9 (12.00)	62 (82.67)	75 (100)	NA
Cough present	3 (4.00)	9 (12.00)	55 (73.33)	67 (89.33)	0.375
Cold/runny nose	3 (4.00)	9 (12.00)	53 (70.67)	65 (86.67)	0.381
Loss of taste	2 (2.67)	0	1 (1.33)	3 (4.00)	<0.001*
Loss of smell	2 (2.67)	0	0	2 (2.67)	<0.001*
Respiratory distress	3 (4.00)	9 (12.00)	18 (24.00)	30 (40.00)	<0.001*
Mild disease	1 (1.33)	0	45 (60.00)	46 (61.33)	<0.001*
Moderate disease	2 (2.67)	9 (12.00)	15 (20.00)	26 (34.67)	
Severe disease	1 (1.33)	0	2 (2.67)	3 (4.00)	

Fever was universal. Cough was present in 67 children (89.33%) and cold/rhinorrhea in 65 (86.67%). Loss of taste and smell were significantly associated with COVID-19 (p<0.001). Respiratory distress was present in 30 children (40%) and was significantly more frequent among COVID-19 and influenza cases (p<0.001). Most Other ILI cases were mild, while COVID-19 and influenza showed relatively greater moderate disease burden.

Table 3: Examination, laboratory and radiological findings

Parameter	COVID	Influenza	Other ILI	Total	p value
HR, mean ± SD	112 ± 17.66	110.22 ± 5.70	108.03 ± 14.68	108.51 ± 13.96	0.800
RR, mean ± SD	32 ± 9.09	34.44 ± 3.28	31.58 ± 9.93	31.95 ± 9.31	0.695
SpO_2, mean ± SD	95 ± 3.56	95.56 ± 1.67	97 ± 1.88	96.72 ± 2.03	0.028*
Raised CRP	4 (5.33)	5 (6.67)	43 (57.34)	52 (69.34)	0.276
Bilateral infiltrates	2 (2.67)	8 (10.67)	12 (16.00)	22 (29.34)	0.003*
Clear chest X-ray	1 (1.33)	1 (1.33)	38 (50.67)	40 (53.33)	

Heart rate and respiratory rate were comparable between groups. Mean SpO_2 was significantly lower in COVID-19 and influenza cases (p=0.028). Raised CRP was observed in 52 children (69.34%), but the difference between disease groups was not significant (p=0.276). Chest radiography showed significant association with disease category; bilateral infiltrates were common in influenza and COVID-19, while clear radiographs predominated in Other ILI (p=0.003).

Table 4: Admission and outcome

Parameter	COVID n (%)	Influenza n (%)	Other ILI n (%)	Total n (%)	p value
Admission required	4 (5.33)	9 (12.00)	21 (28.00)	34 (45.33)	<0.001*
Admission not required	0	0	41 (54.67)	41 (54.67)	

Improved	4 (5.33)	9 (12.00)	62 (82.67)	75 (100)	NA
Not improved	0	0	0	0	

Admission was required in 34 children (45.33%). All COVID-19 and influenza cases required admission, whereas most Other ILI cases were managed on an outpatient basis. This difference was statistically significant ($p<0.001$). All children showed clinical improvement, and no mortality was observed.

Discussion

Influenza-like illness (ILI) remains one of the most common causes of pediatric outpatient visits and hospital admissions worldwide. The present hospital-based cross-sectional study evaluated the clinical profile, inflammatory markers, disease severity, and outcomes among children aged 2 months to 12 years presenting with ILI. The study demonstrated that the majority of cases were classified as non-COVID and non-influenza respiratory illnesses (82.67%), while influenza and COVID-19 accounted for 12% and 5.33% of cases, respectively. These findings support the concept that although COVID-19 and influenza are important causes of respiratory illness, a substantial proportion of pediatric ILI is attributable to other viral pathogens and respiratory infections. Similar observations have been reported in surveillance studies emphasizing the heterogeneity of etiological agents responsible for ILI in children.[1]

The age distribution observed in the present study showed that children aged 1–5 years constituted the largest proportion of cases. Young children are particularly susceptible to respiratory viral infections because of immature immune defenses, close contact in households and educational settings, and limited prior exposure to circulating respiratory viruses. Influenza surveillance data and pediatric epidemiological studies have consistently identified preschool-aged children as a high-risk group for respiratory infections and transmission within the community.[2-4] The comparable age distribution among COVID-19, influenza, and other ILI groups in the present study suggests that age alone may not be useful in differentiating specific etiologies of ILI.

Fever was present in all enrolled children, while cough and rhinorrhea were the next most common symptoms. These findings are consistent with established clinical descriptions of seasonal influenza and pediatric COVID-19, both of which commonly manifest with fever and upper respiratory tract symptoms.[2–6] However, symptom overlap between influenza and COVID-19 remains a major diagnostic challenge. Previous studies comparing COVID-19 and influenza in pediatric populations have reported considerable similarities in presentation, reinforcing the importance of laboratory confirmation for accurate diagnosis.[8,9]

A notable finding of the present study was the significant association of loss of taste and loss of smell with COVID-19 infection. Although these symptoms were observed in a relatively small number of children, they were significantly more common among COVID-19-positive cases than among influenza or other ILI cases. Similar findings have been reported in pediatric COVID-19 literature, where anosmia and ageusia have emerged as characteristic manifestations of SARS-CoV-2 infection, although their prevalence may be underestimated in younger children because of communication limitations.[5,6] Therefore, these symptoms may serve as useful clinical clues when evaluating children with suspected COVID-19.

Respiratory distress was significantly more frequent among children diagnosed with influenza and COVID-19. Additionally, oxygen saturation levels were significantly lower in these groups compared with children suffering from other ILI. These findings indicate greater lower respiratory tract involvement among confirmed influenza and COVID-19 cases. Previous studies have demonstrated that while most pediatric COVID-19 infections are mild, a subset of children can develop significant pulmonary involvement requiring hospitalization and oxygen therapy.[11,13] Likewise, influenza remains an important cause of severe respiratory disease in children, particularly among younger age groups and those with underlying risk factors.[4,14]

Radiological evaluation revealed that bilateral pulmonary infiltrates were significantly more common among COVID-19 and influenza cases, whereas chest radiographs were predominantly normal in children with other ILI. These findings correlate with reports describing viral pneumonic changes associated with both influenza and SARS-CoV-2 infection.[15-17] The overlap of radiological features between these viral infections further highlights the necessity of virological testing and comprehensive clinical assessment for accurate diagnosis and management.[8,14]

The evaluation of inflammatory markers demonstrated that elevated C-reactive protein (CRP) levels were present in nearly two-thirds of the study population. However, CRP levels did not differ significantly between COVID-19, influenza, and other ILI groups. Similar findings have been reported by studies evaluating inflammatory biomarkers in pediatric respiratory infections, suggesting that CRP reflects the intensity of systemic inflammation rather than disease-specific etiology.[7,10] Consequently, CRP may be more useful for assessing disease severity and monitoring clinical response than for differentiating among respiratory viral infections.

The serial evaluation of inflammatory markers among COVID-19 cases demonstrated variable changes in CRP, ferritin, D-dimer, and procalcitonin levels. Although statistical significance could not be established because of the small sample size, increasing ferritin and D-dimer levels observed during follow-up may reflect ongoing inflammatory and prothrombotic responses associated with SARS-CoV-2 infection. Previous studies have highlighted the role of ferritin, D-dimer, and cytokine-mediated inflammatory pathways in severe COVID-19 and hyperinflammatory states.[12] Similarly, laboratory abnormalities including alterations in leukocyte counts and inflammatory markers have been reported among pediatric COVID-19 patients, although their prognostic value remains variable.[7,17] Procalcitonin has also been investigated as a marker of bacterial coinfection and disease severity in febrile children, although its role in distinguishing viral etiologies remains limited.[15]

Hospital admission was significantly more common among children with influenza and COVID-19. This finding is likely attributable to the greater frequency of respiratory distress, hypoxemia, and radiological abnormalities observed in these groups. Nevertheless, all patients in the present study demonstrated clinical improvement and no mortality was recorded. Favorable outcomes may be explained by early diagnosis, prompt supportive care, adherence to institutional management protocols, and timely hospitalization when indicated.

The present study has certain limitations. The relatively small sample size, particularly the limited number of COVID-19-positive cases, may have reduced the statistical power of subgroup analyses. Rapid antigen tests were utilized for diagnosis and may possess lower sensitivity than molecular diagnostic techniques. Furthermore, other respiratory viral pathogens were not systematically identified. Despite these limitations, the study provides valuable information regarding the clinical profile and inflammatory marker patterns among children presenting with ILI and highlights the importance of comprehensive clinical assessment combined with targeted laboratory investigations in pediatric respiratory infections.

Conclusion

Most children presenting with influenza-like illness had non-COVID, non-influenza respiratory illness. Fever, cough and rhinorrhea were the most common symptoms. Loss of taste and smell were significantly associated with COVID-19, while respiratory distress, lower SpO_2, need for admission and bilateral radiological infiltrates were significantly more frequent in COVID-19 and influenza cases. CRP was commonly raised but did not significantly distinguish disease categories. Early clinical assessment, rapid diagnostic testing, severity classification and selective use of inflammatory markers can improve triage and management of children with ILI.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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